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COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                  ENTRY    SESSION
FULL ESTIMATED COST                               11.85     184.16

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)      SINCE FILE      TOTAL
                                                  ENTRY    SESSION
CA SUBSCRIBER PRICE                               -0.78      -0.78

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COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                  ENTRY    SESSION
FULL ESTIMATED COST                               11.85     184.16

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)      SINCE FILE      TOTAL
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CA SUBSCRIBER PRICE                               -0.78      -0.78

FILE 'REGISTRY' ENTERED AT 12:37:14 ON 11 APR 2007
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STRUCTURE FILE UPDATES:    10 APR 2007  HIGHEST RN 929680-66-0
DICTIONARY FILE UPDATES:   10 APR 2007  HIGHEST RN 929680-66-0

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http://www.cas.org/ONLINE/UG/regprops.html

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10613257

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L6      STRUCTURE UPLOADED

=> d 16
L6 HAS NO ANSWERS
L6              STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.


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SAMPLE SEARCH INITIATED 12:37:39 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      384 TO ITERATE

100.0% PROCESSED      384 ITERATIONS                                  5 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          6505 TO     8855
PROJECTED ANSWERS:                5 TO      234

L7            5 SEA SSS SAM L6

=> s 16 full
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FULL SCREEN SEARCH COMPLETED -      7528 TO ITERATE

100.0% PROCESSED     7528 ITERATIONS                                 81 ANSWERS
SEARCH TIME: 00.00.01

L8           81 SEA SSS FUL L6

=> file caplus
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
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FULL ESTIMATED COST                              172.10     356.26

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)      SINCE FILE      TOTAL
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CA SUBSCRIBER PRICE                               0.00      -0.78

FILE 'CAPLUS' ENTERED AT 12:37:46 ON 11 APR 2007
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FILE COVERS 1907 - 11 Apr 2007 VOL 146 ISS 16
FILE LAST UPDATED: 10 Apr 2007 (20070410/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html

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L9 23 L8

=> s l8 full
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=> s l10 py<2003
MISSING OPERATOR L10 PY<2003
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s l10 and py<2003
22870433 PY<2003
L11 14 L10 AND PY<2003

=> d ibib abs hitstr tot

L11 ANSWER 1 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1024194 CAPLUS
DOCUMENT NUMBER: 145:397368
TITLE: Preparation of sulfonyl aryl or heteroaryl hydroxamic acid compounds as matrix metalloprotease inhibitors
INVENTOR(S): Bedell, Louis J.; Mcdonald, Joseph J.; Barta, Thomas E.; Becker, Daniel P.; Shashidhar, Rao N.; Freskos, John N.; Mischke, Brent V.; Getman, Daniel P.; Decrescenzo, Gary A.; Villamil, Clara I.
PATENT ASSIGNEE(S): G. D. Searle & Co., USA
SOURCE: U.S., 162pp., Cont.-in-part of U.S. Ser. No. 310,813.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 11
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 7115632	B1	20061003	US 2000-569034	20000511
US 2001020021	A1	20010906	US 1999-230209	19990624 <--
US 6380258	B2	20020430		
WO 2001085680	A2	20011115	WO 2001-US14706	20010507 <--
WO 2001085680	A3	20020307		

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,

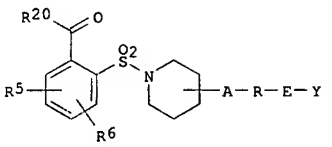
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2003073845	A1	20030417	US 2001-909227	20010719
US 6696449	B2	20040224		

PRIORITY APPLN. INFO.:

US 1999-310813	B2 19990512
US 1999-230209	A2 19990624
US 1997-35182P	P 19970304
WO 1998-US4300	W 19980304
US 2000-569034	A 20000511
US 2000-728408	A2 20001201

OTHER SOURCE(S): MARPAT 145:397368
GI

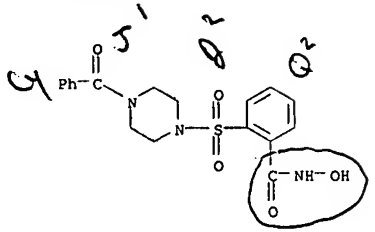


I

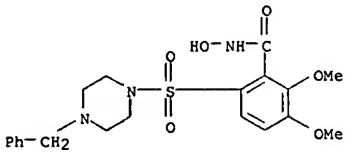
AB The title compds. [I; A = O, S, CO2, etc.; R = alkyl, alkoxyalkyl, aryl, etc.; E = CO, SO2, (un)substituted CONH, etc.; Y = H, alkyl, alkoxy, etc.; R5, R6 = H, alkyl, cycloalkyl, etc.; R20 = OR21, NR13OR22, etc. (R13 = H, alkyl, benzyl; R21 = alkyl, aryl, arylalkyl; R22 = selectively removable protecting group)] or pharmaceutically acceptable salts thereof that inter alia inhibit matrix metalloprotease activity, are prepared Thus, thioetherification of 4-phenoxybenzenethiol with 2-fluorobenzaldehyde in the presence of K2CO3 in isopropanol under reflux for 20 h gave 2-(4-phenoxyphenylthio)benzaldehyde which was condensed with tetra-Et dimethylaminomethylenediphosphonate in the presence of NaH in THF at room temperature for 4 h gave to 2-[2-(4-phenoxyphenylthio)phenyl]acetic acid (II). II was oxidized by H2O2 in acetic acid to 2-[2-(4-phenoxyphenylsulfonyl)phenyl]acetic acid which was condensed with O-tetrahydropyranylhydroxylamine using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride in MeCN followed by treatment with p-toluenesulfonic acid in methanol at room temperature for 2 h to give N-hydroxy-2-[2-(4-phenoxyphenylsulfonyl)phenyl]acetamide (III). III and N-hydroxy-2,3-dimethoxy-6-[[4-[4-(trifluoromethyl)phenoxy]-1-piperidinyl]sulfonyl]benzamide showed IC50 of >10,000 nM against MMP-1, 0.3 and 2.4 nM, resp., against MMP-2, and 2 and 2.7 nM, resp., against MMP-13. Also disclosed is a treatment process that comprises administering a contemplated sulfonyl aromatic or heteroarom. ring hydroxamic acid compound in a matrix metalloprotease (MMP) enzyme-inhibiting effective amount to a host having a condition associated with pathol. MMP activity.

IT 308385-85-5P 308385-86-6P 308385-87-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of sulfonyl aryl or heteroaryl hydroxamic acid compds. as matrix metalloprotease inhibitors)

RN 308385-85-5 CAPLUS
CN Benzamide, 2-[(4-benzoyl-1-piperazinyl)sulfonyl]-N-hydroxy- (9CI) (CA INDEX NAME)



RN 308385-86-6 CAPLUS
CN Benzamide, N-hydroxy-2,3-dimethoxy-6-[[4-(phenylmethyl)-1-piperazinyl]sulfonyl]- (9CI) (CA INDEX NAME)



RN 308385-87-7 CAPLUS
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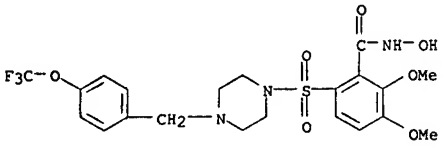

REFERENCE COUNT: 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:300644 CAPLUS
DOCUMENT NUMBER: 138:304308
TITLE: Preparation of sulfonyl aryl hydroxamates and their use as matrix metalloprotease inhibitors
INVENTOR(S): Barta, Thomas E.; Becker, Daniel P.; Bedell, Louis J.; Decrescenzo, Gary A.; Freskos, John N.; Getman, Daniel P.; McDonald, Joseph J.; Mischke, Brent V.; Rao, Shashidhar N.; Villamil, Clara I.
PATENT ASSIGNEE(S): Pharmacia Corp., USA
SOURCE: U.S. Pat. Appl. Publ., 148 pp., Cont.-in-part of U.S. Ser. No. 569,034.

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CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 11
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003073845	A1	20030417	US 2001-909227	20010719
US 6696449	B2	20040224		
WO 9838859	A1	19980911	WO 1998-US4300	19980304 <--
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RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 2001020021	A1	20010906	US 1999-230209	19990624 <--
US 6380258	B2	20020430		
US 7115632	B1	20061003	US 2000-569034	20000511
US 2003191317	A1	20031009	US 2000-728408	20001201
US 6794511	B2	20040921		
CA 2453613	A1	20030130	CA 2002-2453613	20020719
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BR 2002011430	A	20040713	BR 2002-11430	20020719
JP 2005502632	T	20050127	JP 2003-513561	20020719

PRIORITY APPLN. INFO.:		
US 1997-35182P	P	19970304
WO 1998-US4300	W	19980304
US 1999-310813	B2	19990512
US 1999-230209	A2	19990624
US 2000-569034	A2	20000511
US 2000-728408	A2	20001201
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OTHER SOURCE(S): MARPAT 138:304308
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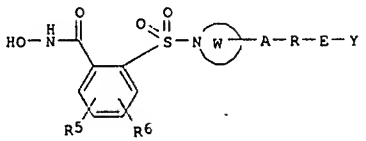

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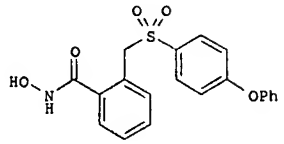


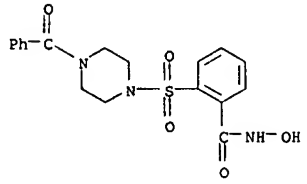
II

AB Title compds. I [W = 6-membered heterocycle containing the sulfonyl bonded N; A-R-E-Y = 4-substituent; A = O, SO0-2, etc.; R = alkyl, alkoxyalkyl, aryl, heteroaryl, cycloalkyl, etc.; E = absent , bond, CO, SO2, etc.; Y = absent, H, OH, CN, NO2, alkyl, haloalkyl, aminoalkyl; R5-6 = together with the atoms to which they are bonded, form an aliphatic or aromatic carbocyclic or heterocyclic ring having 5-7 members] are prepared Over 50 synthetic examples are disclosed. For example, phthalide is reacted with 4-(phenoxy)benzenethiol (DMF, K2CO3, 100°C, 2 h) and the resulting product converted to the hydroxamic acid (CH2Cl2, ClCOCOCl, DMF (cat), TMSONH2, 0°C, 1.5 h) followed by oxidation (CH2Cl2, mCPBA, room temperature, 3 h) to II. II has IC50 = 10 nM for MMP-2, 45 nM for MMP-13 and >10,000 nM for MMP-1. I are inhibitors of MMP and angiogenesis.

IT 308385-85-5P 308385-86-6P 308385-87-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(use of sulfonyl aryl or heteroaryl hydroxamic acids and derivs. as aggrecanase inhibitors)

RN 308385-85-5 CAPLUS

CN Benzamide, 2-[(4-benzoyl-1-piperazinyl)sulfonyl]-N-hydroxy- (9CI) (CA INDEX NAME)



RN 308385-86-6 CAPLUS

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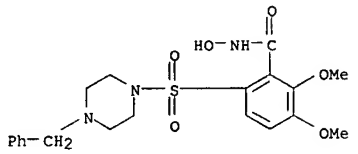
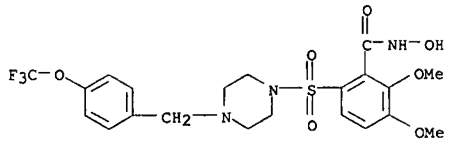
CN Benzamide, N-hydroxy-2,3-dimethoxy-6-[[4-(phenylmethyl)-1-piperazinyl]sulfonyl]- (9CI) (CA INDEX NAME)



RN 308385-87-7 CAPLUS

CN Benzamide, N-hydroxy-2,3-dimethoxy-6-[[4-[[4-(trifluoromethoxy)phenyl]methyl]-1-piperazinyl]sulfonyl]- (9CI) (CA INDEX NAME)



L11 ANSWER 3 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:319307 CAPLUS
DOCUMENT NUMBER: 137:75137
TITLE: Predictions of Binding of a Diverse Set of Ligands to Gelatinase-A by a Combination of Molecular Dynamics and Continuum Solvent Models
AUTHOR(S): Hou, Tingjun; Guo, Senli; Xu, Xiaojie
CORPORATE SOURCE: College of Chemistry and Molecular Engineering, Peking University, Beijing, 100871, Peop. Rep. China
SOURCE: Journal of Physical Chemistry B (2002), 106(21), 5527-5535
CODEN: JPCBFK; ISSN: 1089-5647
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The free energies of binding, ΔGbind, between a diverse set of eight hydroxamate inhibitors with gelatinase-A (MMP-2) were computed by using the recently developed MM/PBSA approach. In this paper, a nonbonded model was used to represent the potentials of the catalytic zinc center. Mol. dynamics (MD) simulations were used to generate the thermally averaged ensemble of conformations of the ligand-protein complexes. On the basis of the trajectories from MD simulations, the free energies of binding were calculated using mol. mechanics, the continuum solvent model, surface area estimation, and normal-mode anal. The results show that MM/PBSA not only can rank the studied ligands effectively but also can reproduce the exptl. binding free energies successfully. The predicted binding free energies correlate well with the exptl. values (r = 0.84, q = 0.78). As a comparison, the free energies of binding were also computed by using the

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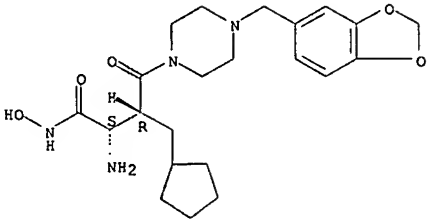
linear interaction energy approximation (LIE). The overall agreement between the calculated and exptl. values for the diverse set of ligands means that the MM/PBSA approach is a useful tool for the general evaluation of protein-ligand interactions. The anal. of the sep. energy terms contributing to MM/PBSA free energy indicates that the association between hydroxamate and MMP-2 is mainly driven by more favorable van der Waals/nonpolar interactions in the complex than in solution

IT 220046-45-7
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(linear interaction energy approximation reveals association between hydroxamate and MMP-2 is promoted by van der Waals/nonpolar interactions in complex than in solution)

RN 220046-45-7 CAPLUS

CN 1-Piperazinebutanamide, α-amino-4-(1,3-benzodioxol-5-ylmethyl)-β-(cyclopentylmethyl)-N-hydroxy-γ-oxo-, (αS,βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 4 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:275960 CAPLUS
DOCUMENT NUMBER: 136:310184
TITLE: Preparation of hydroxamic acid peptide deformylase inhibitors as antibacterial agents
INVENTOR(S): Chong, Lee; Frechette, Roger; Scott, Carole; Tester, Richard; Smith, Whitney; Chiba, Katsumi; Sakamoto, Masatoshi; Gluchowski, Charles
PATENT ASSIGNEE(S): Questcor Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 171 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002028829	A2	20020411	WO 2001-US29926	20010924 <--
WO 2002028829	A3	20031224		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

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CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW

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			US 2001-761850	A 20010118
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OTHER SOURCE(S): MARPAT 136:310184

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Hydroxamic acid derivs. of peptides and peptidomimetics of formulas I, II, and III [wherein Z = NHOH or ORa; Ra = alkyl or a biocleavable moiety; X = CO or SO2; Y = (un)substituted heteroalkyl or heterocyclyl; R1 = (un)substituted (cyclo)alkyl, aryl, heterocyclyl, or heteroalkyl; R2R3 = 4-7 membered (un)substituted heterocycle; R2R4 = ring formed through a CH2CH2 linkage; or R2 = Me; or R3 = H or (un)substituted (hetero)alkyl, aryl, or heterocyclyl; or R4 = H or (un)substituted (hetero)alkyl, aryl, or heterocyclyl; R5 and R6 = independently H, NO2, NH2, NHCOH, NHCOCH3, NHSO2CH3, or (un)substituted CH2NH-(hetero)alkyl or CH2NH-heterocyclyl; one of R7 or R8 = CHR10CONHOH; one of R7 or R8 = (un)substituted (hetero)alkyl, (alkyl)heterocyclyl, or alkylaryl; R9 and R10 = independently H or (un)substituted (hetero)alkyl, (alkyl)heterocyclyl, or alkylaryl] were prepared as peptide deformylase (Fe-PDF) inhibitors for treating various bacterial infections. For example, 3-pyrrolidinol was added to tert-Bu (R)-(2-pentyl)succinate mono(N-hydroxysuccinimide) ester to give the amide (68%). Treatment with 20% TFA/DCM, followed by MeOH, benzene, and TMSN2 in hexanes, to afford the Me ester (90%). The pyrrolidinol was coupled with 4-methoxyphenylisocyanate and the ester converted to the hydroxamic acid (IV) using NH2OH•HCl. The latter inhibited E. coli Fe-PDF with IC50 of 9 nM and showed selectivity for Fe-PDF vs. thermolysin with a selectivity index of 30,000. Thus, I, II, and III are useful as antibiotics against a broad range of infectious disease in animals and humans.

IT 409129-95-9P 409129-96-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(peptide deformylase inhibitor; preparation of hydroxamic acid derivs. of peptides and peptidomimetics as peptide deformylase inhibitors for treatment of infectious diseases)

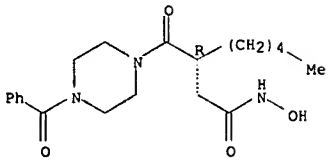
RN 409129-95-9 CAPLUS

CN 1-Piperazinebutanamide, 4-benzoyl-N-hydroxy-γ-oxo-β-pentyl-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

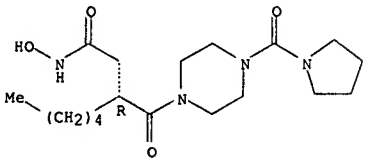
Erich Leeser

50613257



RN 409129-96-0 CAPLUS
CN 1-Piperazinebutanamide, N-hydroxy-γ-oxo-β-pentyl-4-(1-pyrrolidinylcarbonyl)-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:161702 CAPLUS
DOCUMENT NUMBER: 137:5788
TITLE: Binding free energy calculations for MMP2-hydroxamate complexes
AUTHOR(S): Hou, Ting-Jun; Zhang, Wei; Xu, Xiao-Jie
CORPORATE SOURCE: College of Chemistry and Molecular Engineering, Peking University, Beijing, 100871, Peop. Rep. China
SOURCE: Huaxue Xuebao (2002), 60(2), 221-227
CODEN: HHHPA4; ISSN: 0567-7351
PUBLISHER: Kexue Chubanshe
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB The absolute binding affinities of hydroxamate inhibitors with MMP-2 were evaluated by mol. dynamics (MD) simulations with a linear response approach. During MD simulations, a nonbonded model for the catalytic Zn center was used to represent the interactions between Zn center and enzyme/inhibitor. The trajectories from MD simulation show that using the nonbonded model the catalytic Zn ion adopts five coordination number, but the coordination form exists large difference with that of the initial model. After fittings, the models with one parameter, two parameters and three parameters were obtained. The calculated results indicate that the three-parameter model with a constant term bears the best predicting ability. The best model yields an average error of 2.38 kJ/mol for the eight binding affinities of hydroxamates.

IT 220046-45-7
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(binding free energy calcns. for MMP2-hydroxamate complexes)

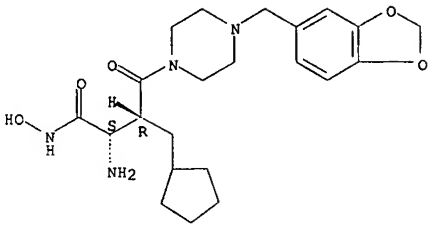
RN 220046-45-7 CAPLUS

Erich Leeser

50613257

CN 1-Piperazinebutanamide, α-amino-4-(1,3-benzodioxol-5-ylmethyl)-β-(cyclopentylmethyl)-N-hydroxy-γ-oxo-, (αS,βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

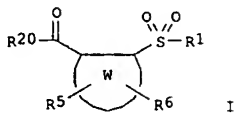


L11 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:833270 CAPLUS
DOCUMENT NUMBER: 135:371526
TITLE: Preparation of sulfonyl aryl or heteroaryl hydroxamic acid compounds as inhibitors of matrix metalloproteinase
INVENTOR(S): Bedell, Louis J.; Mconald, Joseph; Barta, Thomas E.; Becker, Daniel P.; Rao, Shashidhar N.; Freskos, John N.; Mischke, Brent V.; Getman, Daniel P.; Decrescenzo, Gary A.; Villamil, Clara I.
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: PCT Int. Appl., 374 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 11
PATENT INFORMATION:

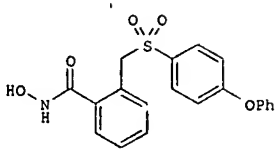
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001085680	A2	20011115	WO 2001-US14706	20010507 <--
WO 2001085680	A3	20020307		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 7115632	B1	20061003	US 2000-569034	20000511
PRIORITY APPLN. INFO.:			US 2000-569034	A 20000511
			US 1999-310813	B2 19990512
			US 1999-230209	A2 19990624

OTHER SOURCE(S): MARPAT 135:371526
GI

Erich Leeser



I



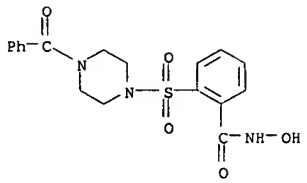
II

AB Title compds. I [W = 5-, 6-membered aromatic or heteroarom. ring; R1 = a substituent containing a 5- or 6-membered cyclohydrocarbyl, heterocyclo, aryl or heteroaryl radical that is bonded directly to the depicted SO2-group said R1 with certain steric requirements; R5-6 = H, alkyl, cycloalkyl, acylalkyl, halo, nitro, hydroxy, cyano, alkoxy, haloalkyl, haloalkyloxy, hydroxyalkyl, etc. or R5-6 together with the atoms to which they are bonded form a further aliphatic or aromatic carbocyclic or heterocyclic ring having 5-to 7-members; R20 = OR21, where R21 = H, alkyl, aryl, arylalkyl, NR13OR22, where R22 = a selectively removable protecting group and R13 = H, alkyl, benzyl group, etc.) were prepared Over 50 synthetic examples were disclosed. For example, phthalide was reacted with 4-(phenoxy)benzenethiol (DMF, K2CO3, 100°C, 2 h) and the resulting product converted to the hydroxamic acid (CH2Cl2, ClCOCOCl, DMF (cat), TMSONH2,0°C, 1.5 h) followed by oxidation (CH2Cl2, mCPBA, room temperature, 3 h) to II. II had IC50 = 10 nM for MMP-2, 45 nM for MMP-13 and >10,000 nM for MMP-1. I are inhibitors of MMP and angiogenesis.

IT 308385-85-5P, 2-[(4-Benzoyl-1-piperazinyl)sulfonyl]-N-hydroxybenzamide 373367-17-0P, N-Hydroxy-2,3-dimethoxy-6-[[4-(phenylmethyl)-1-piperazinyl]sulfonyl]benzamide hydrochloride 373367-18-1P, N-Hydroxy-2,3-dimethoxy-6-[[4-[[4-(trifluoromethoxy)phenyl]methyl]-1-piperazinyl]sulfonyl]benzamide hydrochloride
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug; preparation of sulfonyl aryl or heteroaryl hydroxamic acid compds. as inhibitors of matrix metalloproteinase)

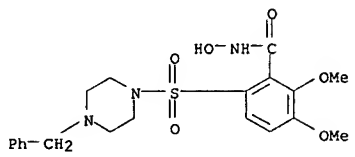
RN 308385-85-5 CAPLUS

CN Benzamide, 2-[(4-benzoyl-1-piperazinyl)sulfonyl]-N-hydroxy- (9CI) (CA INDEX NAME)



RN 373367-17-0 CAPLUS

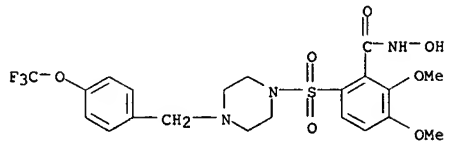
CN Benzamide, N-hydroxy-2,3-dimethoxy-6-[[4-(phenylmethyl)-1-piperazinyl]sulfonyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 373367-18-1 CAPLUS

CN Benzamide, N-hydroxy-2,3-dimethoxy-6-[[4-[[4-(trifluoromethoxy)phenyl]methyl]-1-piperazinyl]sulfonyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L11 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:472692 CAPLUS

DOCUMENT NUMBER: 135:61355

TITLE: Preparation of α-arylethylpiperazine derivatives as neurokinin antagonists

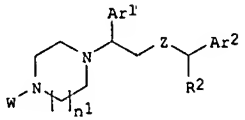
INVENTOR(S): Stiernet, Francoise; Genicot, Christophe; Lassoie, Marie-agnes; Moureau, Florence; Ryckmans, Thomas;

Taverne, Thierry; Henichart, Jean-pierre; Neuwels, Michel; Goldstein, Solo
PATENT ASSIGNEE(S): Ucb, S.A., Belg.
SOURCE: PCT Int. Appl., 115 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001046167	A1	20010628	WO 2000-EP12667	20001214 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1110958	A1	20010627	EP 1999-125359	19991220 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
EP 1242399	A1	20020925	EP 2000-989974	20001214 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003518108	T	20030603	JP 2001-547078	20001214
US 2003220323	A1	20031127	US 2002-168331	20020830
US 6916797	B2	20050712		

PRIORITY APPLN. INFO.: EP 1999-125359 A 19991220
WO 2000-EP12667 W 20001214

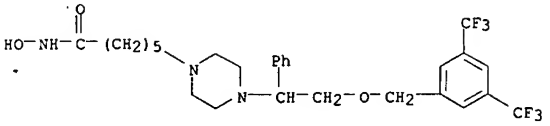
OTHER SOURCE(S): MARPAT 135:61355
GI



I

AB The title compds. [I; Z = O, S; n1 = 1-2; R2 = H, Me; W = cyclohexyl substituted by a CO2H, 2-phenylacetic acid, or alkyl 2-phenylacetate, etc.; Ar1 = (un)substituted Ph, aryl, heteroaryl, etc.; Ar2 = (un)substituted Ph, etc.] and their salts, useful as neurokinin receptor antagonists (NK1antagonists), were prepared Thus, hydrolysis of the corresponding Et ester afforded I [Z = O; R2 = H; n1 = 1; W = (CH2)4CO2H; Ar1 = Ph; Ar2 = 3,5-(F3C)2C6H3] which showed pIC50 of 7.5 against binding to NK1 receptors. The compds. I are useful for the prevention and/or treatment of a condition associated with pathol. levels of substance P.
IT 346416-43-1P 346416-44-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

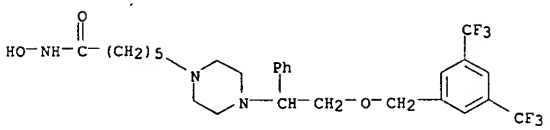
BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of α-arylethylpiperazine derivs. as neurokinin antagonists)
RN 346416-43-1 CAPLUS
CN 1-Piperazinehexanamide, 4-[2-[[3,5-bis(trifluoromethyl)phenyl]methoxy]-1-phenylethyl]-N-hydroxy- (9CI) (CA INDEX NAME)



RN 346416-44-2 CAPLUS
CN 1-Piperazinehexanamide, 4-[2-[[3,5-bis(trifluoromethyl)phenyl]methoxy]-1-phenylethyl]-N-hydroxy-, (2Z)-2-butenedioate (1:2) (salt) (9CI) (CA INDEX NAME)

CM 1

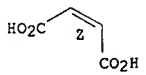
CRN 346416-43-1
CMF C27 H33 F6 N3 O3



CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

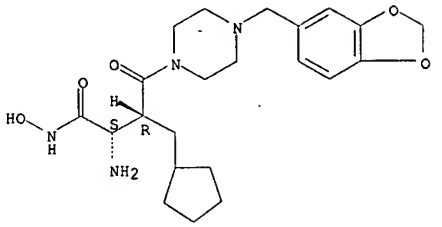
L11 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:390470 CAPLUS
DOCUMENT NUMBER: 135:104175
TITLE: Binding Affinities for a Series of Selective Inhibitors of Gelatinase-A Using Molecular Dynamics

with a Linear Interaction Energy Approach
AUTHOR(S): Hou, T. J.; Zhang, W.; Xu, X. J.
CORPORATE SOURCE: College of Chemistry and Molecular Engineering, Peking University, Beijing, 100871, Peop. Rep. China
SOURCE: Journal of Physical Chemistry B (2001), 105(22), 5304-5315
CODEN: JPCBFK; ISSN: 1089-5647
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The binding of a series of hydroxamate inhibitors with gelatinase-A is examined to evaluate the viability of calculating free energies of binding, ΔGb, utilizing mol. dynamics (MD) simulations with a linear interaction energy approach. In our simulations, a bonded model was used to represent the potentials of the catalytic zinc center. The electrostatic distribution of this model was derived using a two-stage electrostatic potential fitting calcns. The resulting bonded model was then used to generate the MD trajectories. Coulombic, van der Waals, and coordinate bond energy components determined from MD simulations of the bound and unbound inhibitors solvated in water were correlated with the free energies of binding for the 15 hydroxamate inhibitors. In the correlation process, several linear models consisted of different energy components were tested. We found that besides the usually used Coulombic and van der Waals energy terms, the introduction of a constant term could significantly improve the correlation. The best model yields an average error of 0.6 kcal/mol for the 15 binding affinities, which cover an observed range of 7.2 kcal/mol. The predictive ability of the best model was revealed by the high value of q2 (0.854) from the leave-one-out cross-validation. To this series of inhibitors, the constant term can be treated as effective adjustment to the entropy contribution in the binding free energies. The MD simulations predicted the binding mode of the gelatinase-A with the studied inhibitors, and also provided insights into the interactions occurring in the active site and the origins of variations in ΔGb. The P1' groups of inhibitors make extensive van der Waals and hydrophobic contacts with the nonpolar side chains of four residues in the S1' subsite, including Leu 197, Val 198, Leu 218, and Tyr 223, which directly influence the ligand binding. Hydrogen bonds between hydroxamates and gelatinase-A are very important to stabilize the inhibitors in the active site. The hydrogen bonds between the P3' group and gelatinase-A can produce more favorable electrostatic interactions.

IT 220046-45-7
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(binding affinities for a series of selective inhibitors of gelatinase-A using mol. dynamics with a linear interaction energy approach)
RN 220046-45-7 CAPLUS
CN 1-Piperazinebutanamide, α-amino-4-(1,3-benzodioxol-5-ylmethyl)-β-(cyclopentylmethyl)-N-hydroxy-γ-oxo-, (αS,βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

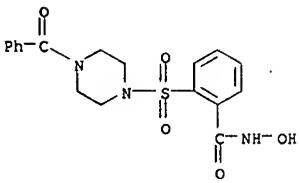


REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:853658 CAPLUS
DOCUMENT NUMBER: 134:222499
TITLE: Synthesis and activity of selective MMP inhibitors with an aryl backbone
AUTHOR(S): Barta, T. E.; Becker, D. P.; Bedell, L. J.; De Crescenzo, G. A.; McDonald, J. J.; Munie, G. E.; Rao, S.; Shieh, H.-S.; Stegeman, R.; Stevens, A. M.; Villamil, C. I.
CORPORATE SOURCE: Pharmacia, Department of Medicinal Chemistry, Skokie, IL, 60077, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2000), 10(24), 2815-2817
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 134:222499

AB A series of novel, MMP-1 sparing arylhydroxamate sulfonamides with activity against MMP-2 and MMP-13 is described. Example compds. thus tested were N-hydroxy-2-[[(phenylmethyl)amino]sulfonyl]benzamide, N-hydroxy-2-[[(4-methoxyphenyl)methylamino]sulfonyl]benzamide, N-hydroxy-2-[[4-(phenylmethyl)-1-piperidinyl]sulfonyl]benzamide, 2-fluoro-N-hydroxy-6-[[4-[4-(trifluoromethyl)phenoxy]-1-piperidinyl]sulfonyl]benzamide, and derivs. or homologs thereof. The crystal and mol. structure of 2-fluoro-N-hydroxy-6-[[4-[4-(trifluoromethyl)phenoxy]-1-piperidinyl]sulfonyl]benzamide compound with MMP-8 were reported.

IT 308385-85-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
((aminosulfonyl)-N-hydroxybenzamide derivs. and their activity as gelatinase (MMP-2) and collagenase (MMP-13) inhibitors)
RN 308385-85-5 CAPLUS
CN Benzamide, 2-[(4-benzoyl-1-piperazinyl)sulfonyl]-N-hydroxy- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:824218 CAPLUS
DOCUMENT NUMBER: 134:4752
TITLE: Preparation of hydroxamic acid derivatives as matrix metalloprotease inhibitors
INVENTOR(S): Bedell, Louis J.; McDonald, Joseph J.; Barta, Thomas E.; Becker, Daniel P.; Rao, Shashidhar N.; Freskos, John N.; Mischke, Brent V.; Getman, Daniel P.; Decrescenzo, Gary A.; Villamil, Clara I.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: PCT Int. Appl., 380 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 11
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000069819	A1	20001123	WO 2000-US6713	20000512 <--
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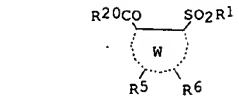
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2373500	A1	20001123	CA 2000-2373500	20000512 <--
EP 1177173	A1	20020206	EP 2000-931910	20000512 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000011291	A	20020514	BR 2000-11291	20000512 <--
JP 2002544257	T	20021224	JP 2000-618236	20000512 <--
NZ 515197	A	20040326	NZ 2000-515197	20000512
AU 781339	B2	20050519	AU 2000-49718	20000512
ZA 2001009007	A	20030131	ZA 2001-9007	20011031
PRIORITY APPLN. INFO.:			US 1999-310813	A 19990512
			WO 2000-US6713	W 20000512

OTHER SOURCE(S): MARPAT 134:4752
GI

Erich Leeser



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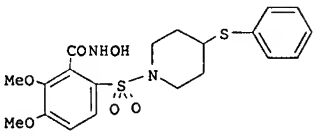
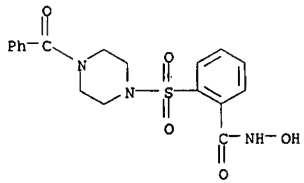


II

AB Title compds. [I; W = 5, 6 membered aromatic, heteroarom. ring; R = 5, 6 membered cyclohydrocarbyl, heterocyclo, aryl, heteroaryl; R5. R6 independently = hydrido, alkyl, cycloalkyl, acylalkyl, halo, nitro, hydroxyl, cyano, alkoxy, haloalkyl, haloalkyloxy, hydroxyalkyl, etc; R20 = alkoxy, aryloxy, alkoxyamino, benzyloxyamino, etc] and pharmaceutically acceptable salts with inter alia inhibits matrix metalloprotease activity are disclosed and a treatment that comprises administering a contemplated sulfonyl aromatic or heteroarom. hydroxamic acid in an MMP enzyme-inhibiting effective amount to a host having a condition associated with pathol. matrix metalloprotease activity are claimed. Thus, the title compound II was prepared and MMP-2, MMP-3, MMP-8, MMP-13, and MT1-MMP inhibition activities were assayed.

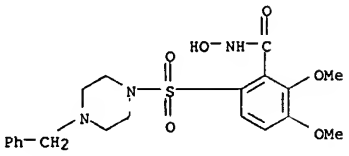
IT 308385-85-5P 308385-86-6P 308385-87-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of hydroxamic acid derivs. as matrix metalloprotease inhibitors)

RN 308385-85-5 CAPLUS
CN Benzamide, 2-[(4-benzoyl-1-piperazinyl)sulfonyl]-N-hydroxy- (9CI) (CA INDEX NAME)

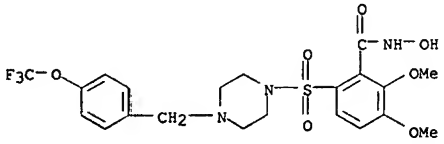


RN 308385-86-6 CAPLUS
CN Benzamide, N-hydroxy-2,3-dimethoxy-6-[[4-(phenylmethyl)-1-piperazinyl]sulfonyl]- (9CI) (CA INDEX NAME)

Erich Leeser



RN 308385-87-7 CAPLUS
CN Benzamide, N-hydroxy-2,3-dimethoxy-6-[[4-[[4-(trifluoromethoxy)phenyl]methyl]-1-piperazinyl]sulfonyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:441768 CAPLUS
DOCUMENT NUMBER: 133:74324
TITLE: Preparation of amino acid sulfonamide hydroxamates as inhibitors of procollagen C-proteinase.
INVENTOR(S): Billedeau, Roland Joseph; Broka, Chris Allen; Campbell, Jeffrey Allen; Chen, Jian Jeffrey; Dankwardt, Sharon Marie; Delaet, Nancy; Robinson, Leslie Ann; Walker, Keith Adrian Murray
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
SOURCE: PCT Int. Appl., 133 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000037436	A1	20000629	WO 1999-EP9920	19991214 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2355902	A1	20000629	CA 1999-2355902	19991214 <--
BR 9916504	A	20010911	BR 1999-16504	19991214 <--

Erich Leeser

EP 1149072	A1	20011031	EP 1999-963530	19991214 <--
EP 1149072	B1	20040630		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200101868	T2	20011121	TR 2001-200101868	19991214 <--
HU 200104658	A2	20020629	HU 2001-4658	19991214 <--
JP 2002533322	T	20021008	JP 2000-589508	19991214 <--
AU 769319	B2	20040122	AU 2000-19792	19991214
NZ 512292	A	20040326	NZ 1999-512292	19991214
AT 270271	T	20040715	AT 1999-963530	19991214
RU 2232751	C2	20040720	RU 2001-119461	19991214
US 6492394	B1	20021210	US 1999-469660	19991222 <--
HR 2001000443	A1	20020630	HR 2001-443	20010614 <--
ZA 2001005014	A	20020919	ZA 2001-5014	20010619 <--
IN 2001CN00859	A	20050304	IN 2001-CN859	20010620
NO 2001003100	A	20010821	NO 2001-3100	20010621 <--
US 2003199520	A1	20031023	US 2002-267292	20021009
US 6844366	B2	20050118		
US 2003216405	A1	20031120	US 2002-267727	20021009
US 6787559	B2	20040907		

PRIORITY APPLN. INFO.:

US 1998-113311P	P	19981222
US 1999-147053P	P	19990803
US 1999-164138P	P	19991108
WO 1999-EP9920	W	19991214
US 1999-469660	A3	19991222

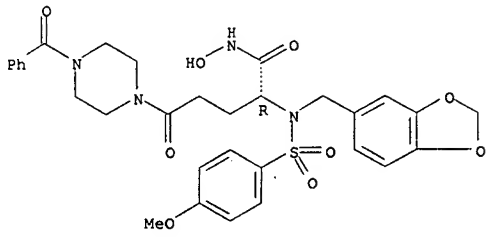
OTHER SOURCE(S): MARPAT 133:74324

AB HOHNCOCHR1NRSO2Ar2 [R1 = alkyl, haloalkyl, heteroalkyl, cycloalkyl, aryl, aralkyl, aralkenyl, heteroaryl, heteroaralkyl, aminl, aryl, aralkyl, etc.; R = CHR2Ar1, CHR2CH:CHAr1; Ar2 = specified (substituted) Ph, naphthyl; R2 = H, alkyl; with provisos], were prepared Thus, N-hydroxy-2(R)-[(3,4-methylenedioxybenzyl)(4-methoxy-2,3,6-trimethylbenzenesulfonyl)amino]-3-methylbutyramide was prepared by solution phase synthesis from BOC-D-Val-OH. Title compds. inhibited procollagen C-proteinase with IC50 0.01-2 μM.

IT 279255-56-0P 279255-58-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amino acid sulfonamide hydroxamates as inhibitors of procollagen C-proteinase)

RN 279255-56-0 CAPLUS
CN 1-Piperazinepentanamide, α-[(1,3-benzodioxol-5-ylmethyl)[(4-methoxyphenyl)sulfonyl]amino]-4-benzoyl-N-hydroxy- δ-oxo-, (αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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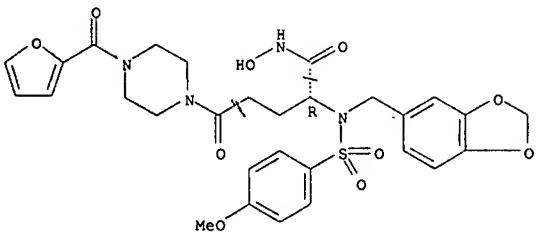
RN 279255-58-2 CAPLUS
CN 1-Piperazinepentanamide, α-[(1,3-benzodioxol-5-ylmethyl)[(4-methoxyphenyl)sulfonyl]amino]-4-(2-furanylcarbonyl)-N-hydroxy- δ-oxo-, (αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



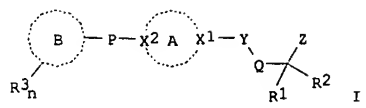
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:161258 CAPLUS
DOCUMENT NUMBER: 132:207849
TITLE: Preparation of arylpiperazines as metalloproteinase inhibiting agents (MMP)
INVENTOR(S): Barlaam, Bernard Christophe; Newcombe, Nicholas John; Tucker, Howard; Waterson, David
PATENT ASSIGNEE(S): Zeneca Limited, UK; Zeneca-Pharma Sa
SOURCE: PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 2000012478	A1	20000309	WO 1999-GB2801	19990825	<--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW					
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
CA 2339761	A1	20000309	CA 1999-2339761	19990825	<--
AU 9955247	A	20000321	AU 1999-55247	19990825	<--
AU 764367	B2	20030814			
BR 9913255	A	20010522	BR 1999-13255	19990825	<--
EP 1109787	A1	20010627	EP 1999-941751	19990825	<--
EP 1109787	B1	20060517			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY					

TR 200100605	T2	20010821	TR 2001-200100605	19990825	<--
HU 200103344	A2	20020228	HU 2001-3344	19990825	<--
EE 200100106	A	20020617	EE 2001-106	19990825	<--
JP 2002523493	T	20020730	JP 2000-567511	19990825	<--
NZ 509730	A	20030530	NZ 1999-509730	19990825	
RU 2220967	C2	20040110	RU 2001-108591	19990825	
NZ 524921	A	20041029	NZ 1999-524921	19990825	
AT 326448	T	20060615	AT 1999-941751	19990825	
PT 1109787	T	20060929	PT 1999-941751	19990825	
ES 2263284	T3	20061201	ES 1999-941751	19990825	
TW 240722	B	20051001	TW 1999-88114833	19990830	
ZA 2001001231	A	20020513	ZA 2001-1231	20010213	<--
US 6734184	B1	20040511	US 2001-763709	20010226	
NO 2001001023	A	20010425	NO 2001-1023	20010228	<--
NO 321478	B1	20060515			
BG 105369	A	20011231	BG 2001-105369	20010322	<--
HK 1036060	A1	20061027	HK 2001-106732	20010924	
AU 2003262101	A1	20031218	AU 2003-262101	20031112	
US 2004171641	A1	20040902	US 2004-787775	20040226	
PRIORITY APPLN. INFO.:			EP 1998-402144	A 19980831	
			EP 1999-401351	A 19990604	
			WO 1999-GB2801	W 19990825	
			US 2001-763709	A1 20010226	

OTHER SOURCE(S): MARPAT 132:207849
GI



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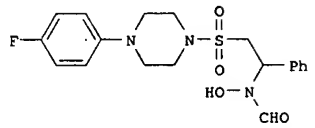


II

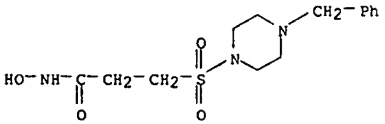
AB The title compds. [I; B = monocyclic or bicyclic alkyl, aryl, etc.; R3 = H, halo, NO2. etc.; n = 1-3; P = (CH2)n (wherein n = 0-2), alkene, alkyne, etc.; A = (un)substituted 5-7 membered aliphatic ring; X1, X2 = N, C, where a ring substituent on ring A is a oxo group that is preferably adjacent a ring N atom; Y = SO2, CO; Z = CONHOH, Y = CO and Q = CR6R7, CR6R7CH2, NR6, NR6CH2 (wherein R6 = H, alkyl, aralkyl, etc.; R7 = H, alkyl; R7 together with R6 forms a carbocyclic or heterocyclic spiro 5-7 membered ring, the latter containing at least one heteroatom selected from N, O, S); Z = CONHOH, Y = SO2 and Q = CR6R7, CR6R7CH2; Z = N(OH)CHO and Q = CHR6, CHR6CH2, NR6CH2; R1 = H, alkyl, cycloalkyl, etc.; R2 = H, alkyl, aryl, etc.], useful as metalloproteinase inhibitors (no data), especially as inhibitors of

MMP 13, in treating arthritis and atherosclerosis, were prepared E.g., a multi-step synthesis of the title piperazine II was given. Compds. I are effective at 0.5-30 mg/kg/day.

IT 260438-45-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of arylpiperazines as metalloproteinase inhibiting agents (MMP))

RN 260438-45-7 CAPLUS

CN Propanamide, N-hydroxy-3-[[4-(phenylmethyl)-1-piperazinyl]sulfonyl]- (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:64787 CAPLUS

DOCUMENT NUMBER: 130:139360

TITLE: Preparation of succinyl piperidinamides, morpholinamides, piperazinamides, and analogs as matrix metalloproteinase inhibitors

INVENTOR(S): Alpegiani, Marco; Bissolino, Pierluigi; Abrate, Francesca; Perrone, Ettore; Corigli, Riccardo; Jabes, Daniela

PATENT ASSIGNEE(S): Pharmacia & Upjohn S.P.A., Italy

SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9902510	A1	19990121	WO 1998-EP4220	19980707 <--
W: AL, AU, BR, CA, CN, CZ, HU, ID, IL, JP, KR, MX, NO, NZ, PL, RO, UA, US, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2265671	A1	19990121	CA 1998-2265671	19980707 <--
AU 9888583	A	19990208	AU 1998-88583	19980707 <--
EP 925289	A1	19990630	EP 1998-940170	19980707 <--
R: DE, ES, FR, GB, IT, SE				
JP 2001500533	T	20010116	JP 1999-508146	19980707 <--
US 6482827	B1	20021119	US 1999-147798	19990310 <--

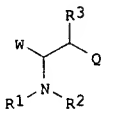
PRIORITY APPLN. INFO.:

GB 1997-14548	A	19970710
GB 1997-24395	A	19971118
WO 1998-EP4220	W	19980707

Erich Leeser

OTHER SOURCE(S): MARPAT 130:139360

GI



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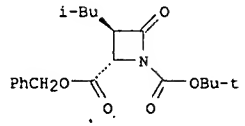
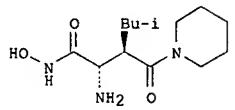


II



III

AB Title compds. I [W = CONHOH or COOH; R1 and R2 = H or an organic residue; R3 = organic group; Q = secondary or tertiary acyclic or cyclic amido group] and their pharmaceutically acceptable salts, solvates, and hydrates are disclosed as inhibitors of matrix metalloproteinases (MMPs), and of the release of tumor necrosis factor-alpha (TNF) from cells. The compds. are therefore useful in the prevention, control and treatment of diseases in which MMPs or TNF are involved, especially tumoral and inflammatory diseases. Processes for their preparation, and pharmaceutical compns. containing them are also described. For instance, the intermediate 4(S)-(benzyloxycarbonyl)-1-(tert-butoxycarbonyl)-3(R)-isobutylazetidin-2-one (II; preparation given) was subjected to a sequence of ring opening/amidation with piperidine, followed by hydrogenolytic deprotection of the benzyl ester, amidation with PhCH2ONH2.HCl, another hydrogenolysis of the benzyl ether, and acidic deprotection of the BOC-amino group, to give title compound III. The latter compound showed superior aqueous solubility (> 9.5 mg/mL at 25°), and had Ki values as follows: MMP-1 0.088, MMP-2 0.29, and MMP-3 2.5, all in μM.

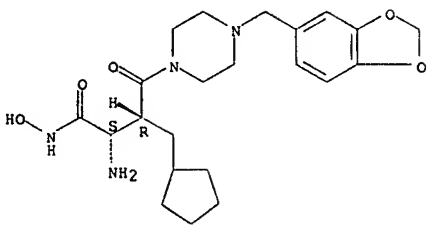
IT 220046-45-7P
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent); USES (Uses)
(target compound; preparation of succinyl piperidinamides, morpholinamides, and piperazinamides as matrix metalloproteinase inhibitors)

RN 220046-45-7 CAPLUS

CN 1-Piperazinebutanamide, α-amino-4-(1,3-benzodioxol-5-ylmethyl)-β-(cyclopentylmethyl)-N-hydroxy-γ-oxo-, (αS,βR)- (9CI) (CA INDEX NAME)

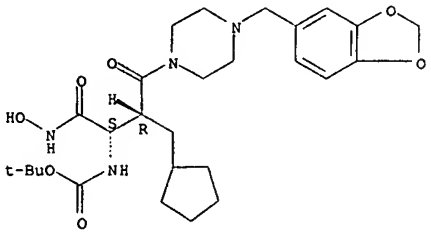
Absolute stereochemistry.

Erich Leeser



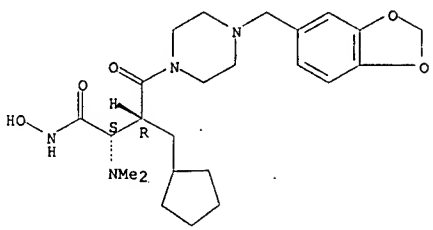
IT 220046-44-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(target compound; preparation of succinyl piperidinamides, morpholinamides, and piperazinamides as matrix metalloproteinase inhibitors)
RN 220046-44-6 CAPLUS
CN Carbamic acid, [(1S,2R)-3-[4-(1,3-benzodioxol-5-ylmethyl)-1-piperazinyl]-2-(cyclopentylmethyl)-1-[(hydroxyamino)carbonyl]-3-oxopropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



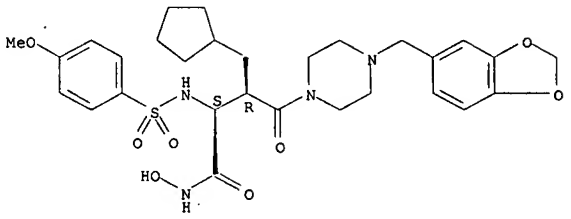
IT 220046-55-9P 220046-57-1P 220046-70-8P
220046-82-2P 220046-88-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compound; preparation of succinyl piperidinamides, morpholinamides, and piperazinamides as matrix metalloproteinase inhibitors)
RN 220046-55-9 CAPLUS
CN 1-Piperazinebutanamide, 4-(1,3-benzodioxol-5-ylmethyl)-β-(cyclopentylmethyl)-α-(dimethylamino)-N-hydroxy-γ-oxo-, (αS,βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 220046-57-1 CAPLUS
CN 1-Piperazinebutanamide, 4-(1,3-benzodioxol-5-ylmethyl)-β-(cyclopentylmethyl)-N-hydroxy-α-[[(4-methoxyphenyl)sulfonyl]amino]-γ-oxo-, (αS,βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

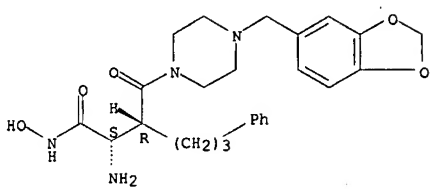


RN 220046-70-8 CAPLUS
CN 1-Piperazinebutanamide, α-amino-4-(1,3-benzodioxol-5-ylmethyl)-N-hydroxy-γ-oxo-β-(3-phenylpropyl)-, (αS,βR)-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

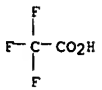
CRN 220046-69-5
CMF C25 H32 N4 O5

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

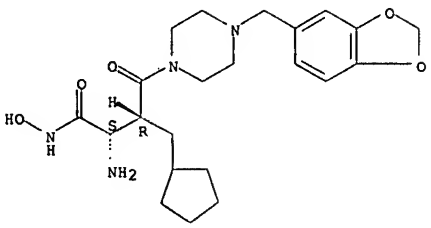


RN 220046-82-2 CAPLUS
CN 1-Piperazinebutanamide, α-amino-4-(1,3-benzodioxol-5-ylmethyl)-β-(cyclopentylmethyl)-N-hydroxy-γ-oxo-, (αS,βR)-, bis(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

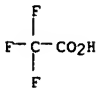
CRN 220046-45-7
CMF C22 H32 N4 O5

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



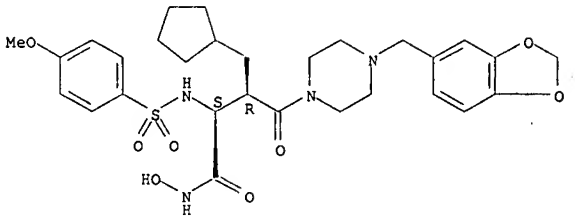
RN 220046-88-8 CAPLUS
CN 1-Piperazinebutanamide, 4-(1,3-benzodioxol-5-ylmethyl)-β-(cyclopentylmethyl)-N-hydroxy-α-[[(4-methoxyphenyl)sulfonyl]amino]-γ-oxo-, (αS,βR)-, mono(trifluoroacetate) (salt) (9CI)

(CA INDEX NAME)

CM 1

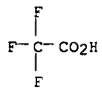
CRN 220046-57-1
CMF C29 H38 N4 O8 S

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1979:604719 CAPLUS
DOCUMENT NUMBER: 91:204719
TITLE: Pharmaceutical compositions containing piperazinyl acylhydroxamic acid derivatives to treat inflammation or anaphylactic allergy conditions
INVENTOR(S): Coutts, Ronald T.; Biggs, David F.; Wandelmaier, Frank W.; Semaka, Frank D.
PATENT ASSIGNEE(S): Canadian Patents and Development Ltd., Can.
SOURCE: U.S., 5 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4166116	A	19790828	US 1977-850825	19771111 <--

50613257

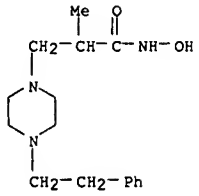
CA 1095832 A1 19810217 CA 1978-315010 19781031 <--
PRIORITY APPLN. INFO.: US 1977-850825 A 19771111
OTHER SOURCE(S): MARPAT 91:204719
GI

I

AB Seven piperazinylacylhydroxamic acids I [X = straight or branched C1-3 alkylene, m = 0, 1, or 2, Y = a salt forming acid (when present)] derivs. were prepared by aminoesterification of the corresponding 1-monosubstituted piperazines and then converted to the HCl salts. The compds. showed antiinflammatory, antianaphylactic, and antidepressant activities. Thus, 2-methyl-3-[1-(4-phenyl)piperazinyl]propionohydroxamic acid-HCl [71861-77-3] inhibited carrageenan-induced edema volume by 23.5% 1 h after s.c. administration to rats, decreased egg albumin-induced anaphylaxis by 72% when given i.v. to rats (50 mg/kg), and protected 92% of reserpinized rats given 32 mg of the compound/kg, i.p.

IT 71861-78-4P 71861-81-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and antiinflammatory and antianaphylactic activity of)

RN 71861-78-4 CAPLUS
CN 1-Piperazinepropanamide, N-hydroxy-α-methyl-4-(2-phenylethyl)-, monohydrochloride (9CI) (CA INDEX NAME)

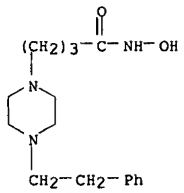


● HCl

RN 71861-81-9 CAPLUS
CN 1-Piperazinebutanamide, N-hydroxy-4-(2-phenylethyl)-, dihydrochloride (9CI) (CA INDEX NAME)

Erich Leeser

50613257



● 2 HCl

=> FIL STNGUIDE

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	77.20	433.46
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-10.92	-11.70

FILE 'STNGUIDE' ENTERED AT 12:39:29 ON 11 APR 2007

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Apr 6, 2007 (20070406/UP).

Erich Leeser